UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,793	10/24/2003	Jerome B. Zeldis	9516-080-999	2026

20583 7590 10/18/2007

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,793	ZELDIS ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *3-21,24,25 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,22,23 and 26-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/30/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed July 30, 2007 have been received and entered into the application.

Action Summary

The rejection of claims 1, 2, 22, 23 and 26-35 under 35 U.S.C. 112, first paragraph (enablement) is being maintained for the reasons stated in the previous Office Action.

The rejection of claims 1, 28-35 under 35 U.S.C. 102(e) as being anticipated by Bhagwat et al. (U.S.Patent No. 6,897,231 B2) is being maintained for the reasons stated in the previous Office Action.

The rejection of claims 1, 28-31 under 35 U.S.C. 102(e) as being anticipated by Bhagwat et al. (U.S.Patent No. 6,897,231 B2) evidenced by Sanders et al. (U.S. patent No. 5,766,605 A) or Mathias (U.S. patent No. 5,4341,36A) is being maintained for the reasons stated in the previous Office Action.

The rejection of claims 1, 28-31 under 35 U.S.C. 102(e) as being anticipated by Stein et al. (US 2004/0067953A1) is being maintained for the reasons stated in the previous Office Action.

The rejection of claims 1, 2, 22, 23 and 26-35 under 35 U.S.C. 103(a) as being unpatentable over Stein et al. (US 2004/0067953A1) in view of Graczyk et al. (WO 02/081475 A1) is hereby expressly withdrawn in view of Applicant's persuasive argument.

Applicants' amendment necessitated additional rejection presented in this Office action.

Response to Arguments

Applicants' arguments filed July 30, 2007 have been fully considered but they are not persuasive. Applicants argue that the examples of in Sections 5.1-5.4 at pages 67-70 are directed to the prevention of pain because that each example teach that the JNK inhibitor is administered prior to the inducement of pain (e.g., by formalin injection, hot plate, tail-flick or topical capsaicin). The examples have been carefully reviewed and considered. However, it is not persuasive. Although, the examples may comprise the step of administering JNK inhibitors prior to the inducement of pain, it does not show the absolute prevention of pain so that pain never develops. It is noted that the example 5.1 indicate that the animal is observed for 10 minutes after injection of formalin and the number of times the animal flinches the injected paw were still counted. Further, Applicants' admit that there is a drawback with animal model is that they can only measure evoked pain and that no animal model is able to measure spontaneous pain which is one of the most concerning in connection with clinical pain states. (instant

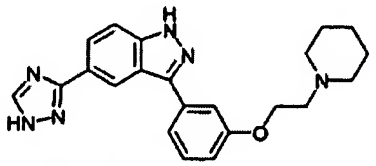
specification, paragraph before Example 5.1). To the extent that the instant claims are drawn to an absolute "prevention", which is highly speculative, a greater amount of evidence is required to show its operability in humans. Therefore, Applicants' absolute prevention of pain, particularly, spontaneous pain, by administration of the instant JNK inhibitors claimed by Applicants is not enabled by the instant specification as filed. Applicants essentially argue that the literature references and examples discussed above demonstrate that pain and any underlying condition are separate entities with respect to their treatment and that pain itself should be considered as a disease in its own right. This is not persuasive because the instant claims are drawn to "..**preventing**.. pain .... in a patient **in need thereof**...". Therefore, the cited reference (Bhagwat et al. U.S.Patent No. 6,897,231 B2) clearly teaches the administration of the same active agent to the same subject population who are in "need" of preventing pain. It is noted that Bhagwat et al teaches the treatment of diabetes and cancers that is related to pain. (see also Applicants' claim 31 "cancer-related pain", "diabetic neuropathy"). Accordingly, upon the administration of the same active agents to the same subject population of Bhagwat et al. who are in "need" of preventing pain (cancer-related pain or diabetic neuropathy), the instantly claimed pain would be inherently prevented/treated by removing/treating the underlining diseases causing pain. Applicants argue that autonomic dysfunction can be a component of certain diseases but not a type of disease (asthma and lupus erythematosus) implied by the Examiner and that these disease are not "autonomic dysfunctions". This is not found persuasive because both of references cited in the previous Office Action clearly teaches that

asthma and Lupus Erythematosus are dysfunctions of autonomic system ant that Applicants do not disagree that the disease such as asthma and lupus erythematosus exhibit "autonomic dysfunction". The issue is not whether the asthma is involved with a dysfunction of an autonomic nerve component, but that disorder of asthma is involved/encompassed with "autonomic dysfunction" in general. Therefore, the teachings of Bhagwat et al. for the **treatment** and **prevention** of lupus erythematosus and asthma clearly anticipates claimed invention. Applicants argue that Stein et al.'s teaching of the treatment of cancer does not anticipate the treatment of pain associated with cancer. This is not persuasive because stein et al. clearly teaches the administration of the same active agent to the same subject population who are in "need" of **preventing/treating** cancer **pain**. It is noted that Stein et al. teaches the treatment of cancers that is related to pain. (see Applicants' claim 31 "cancer-related pain"). Accordingly, upon the administration of the same active agents to the same subject population of Stein et al. who are in "need" of **preventing/treating** pain (cancer-related pain), the instantly claimed pain would be **prevented/treated** by removing/treating the underlining disease (cancer) causing pain. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

In view of the above Office Action of May 3, 2007 is deemed proper and asserted with full force and repeated herein.

Applicant's are reminded of Applicants' election **without traverse** of Group I, claims 1, 2, 5-11, 22, 23 and 26-35 drawn to a method for treating, preventing managing

and/or modifying pain in a patient, comprising administering to a patient in need there of an effective amount of a compound having the formula set forth in claims 2, 5-11 and 23 with an election of species of 3-(3-(2-(piperidin-1-yl)ethoxy)phenyl)-5-(1H-1,2,4-triazol-3-yl)-1H-1H-indazole having the following structure:



3-[3-(2-Piperidin-1-yl-ethoxy)-phenyl]-5-(1*H*-[1,2,4]triazol-3-yl)-1*H*-indazole ;

Claims 1, 2, 22, 23 and 26-35 have been examined only to the extent of applicants' elected species of 3-(3-(2-(piperidin-1-yl)ethoxy)phenyl)-5-(1H-1,2,4-triazol-3-yl)-1H-1H-indazole.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation of "**..pain is... lost hair, dry hand, color change to the skin, weakness, edema, increased sweating..etc**" renders the claim vague and indefinite because above conditions that equates the term "pain" where applicants act as his or her own lexicographer to specifically define a term of a claim **contrary to its ordinary meaning**, the written description must clearly redefine the claim term and set forth the

uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term ""**pain**" in claim 31 is used by the claim to mean "**lost hair, dry hand, color change to the skin, weakness, edema, increased sweating..etc**", while the accepted meaning is "pain, hyperalgesia, nociception etc.." The term is indefinite because the specification does not clearly redefine the term.

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2, 22, 23 and 26-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treatment of pain", does not reasonably provide enablement for the "**preventing** pain". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors**

have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method for treating, preventing, managing and/or modifying pain in a patient, comprising administering to a patient in need thereof an effective amount of a JNK inhibitor or a pharmaceutically acceptable salt, solvate or stereoisomer thereof. The nature of the invention is extremely complex in that it encompasses the actual prevention of painful disorder (i.e. break though pain, neuropathic pain) such that the subject treated with above compounds does not contract pain.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass prevention of painful disorder in humans which has potentially many different causes (i.e. many different neuropathy including resulting from chemotherapy or combination of diseases). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually prevent pain is minimal. All of the guidance provided by the specification is directed towards treatment rather than **prevention** of pain.

Working Examples: All of the working examples provided by the specification are directed toward the treatment rather than prevention of pain.

State of the Art: While the state of the art is relatively high with regard to treatment of pain (i.e. cancer pain, lower back pain), the state of the art with regard to prevention of such disorders is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to prevent development of pain. The state of the art, Shah et al. (U.S.Patent 6,562,033 B2) teaches that making treatment and management of lower back pain is very difficult. (column 1, lines 20-30).

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual prevention of pain in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of prevention of pain.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for prevention of pain. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard prevention of pain with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of

treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of pain with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of pain in a subject by administration of one of the claimed compounds.

Therefore, a method for treating, **preventing**, managing and/or modifying pain in a patient, comprising administering to a patient in need thereof an effective amount of a JNK inhibitor or a pharmaceutically acceptable salt, solvate or stereoisomer thereof, is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 28-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Bhagwat et al. (U.S.Patent No. 6,897,231 B2).

Bhagwat et al. teach that Applicants active agent is useful for the treatment of stroke, asthma, osteoarthritis, rheumatoid arthritis and lupus erythematosus, diabetes and cancers of a variety of tissues.

Applicants claiming "complex regional pain syndrome" are "cancer-related pain"; Applicants claiming "nociceptive pain" are "associated" with osteoarthritis and rheumatoid arthritis; Applicants claiming "neuropathic pain" are "associated" with stroke, and diabetic neuropathy.

Accordingly, above teaching of Bhagwat et al. clearly prevented pain associated with the diseases above by preventing or treating the diseases that causes pain. Therefore, Bhagwat et al. clearly anticipates Applicants' claiming invention.

Claims 1, 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Bhagwat et al. (U.S.Patent No. 6,897,231 B2) evidenced by Sanders et al. (U.S. patent No. 5,766,605 A) or Mathias (U.S. patent No. 5,4341,36A).

Bhagwat et al. teach that Applicants active agent is useful for the treatment and prevention of lupus erythematosus and asthma.

Applicants claiming the treatment/prevention of pain is a "complex regional pain syndrome" as an **autonomic dysfunction**.

Sanders et al. teach that asthma is autonomic dysfunction. (abstract, claim 1)

Mathias teaches that Lupus Erythematosus is an autonomic dysfunction. (column 1, lines 11-20).

Therefore, Bhagwat et al. clearly anticipates Applicants' claiming invention.

Claims 1, 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Stein et al. (US 2004/0067953A1).

Stein et al. teach the treatment and prevention of cancer by the administration of an effective amount of Applicant's active agent. (abstract, Figure 6, C).

Applicants claiming "complex regional pain syndrome" are "cancer-related pain".

Accordingly, above teaching of Stein et al. clearly prevented pain associated with cancer by preventing or treating cancer that causes pain. Therefore, Stein et al. clearly anticipates Applicants' claiming invention.

None of the claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Kim
Primary Examiner
Art Unit 1617

Jmk
October 11, 2007